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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,167	05/25/2006	Jean-Yves Chane-Ching	99342.00073US	3655

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EXAMINER	
WANG, CHUN CHENG	

ART UNIT	PAPER NUMBER
1796	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,167	CHANE-CHING, JEAN-YVES	
	Examiner	Art Unit	
	Chun-Cheng Wang	1796	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14-19* is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to the Amendment filed on 06/02/2009. Claim 20 has been cancelled. Claims 1-19 are now pending.

2. The objections and rejections not addressed below are deemed withdrawn. The following rejections are based on the new ground. Therefore, this Office Action is made as 2nd non-final.

3. The text of those sections of Title 35, U.S. Code not included in this section can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

4. Claims 1-6 and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itoi et al. (US6159437) in view of Kumta et al. (US7247288).

Claims 1-4: Itoi et al. disclose an apatite dispersion with polymeric phosphate dispersion agents such as sodium hexametaphosphate and sodium tripolyphosphate (column 3 lines 53 and 54) and the size of the apatite particle is 10-100 nm in short-axis and 30-300 nm in long axis (a prima facie case of obviousness, since the claimed ranges "overlap or lie inside ranges disclosed by the prior art", read on claims 1-3) (column 3 lines 22-24).

Itoi et al. is silent on polymer which complexes calcium.

Kumta et al. disclose a method for production of nanocrystalline hydroxyapatite particles comprising polymers complex calcium phosphate which include polyamino acids (column 9, lines 43-44), such as poly-L-lysine and polyacrylate (column 9, line 48). The nanocrystalline hydroxyapatite particles exhibit substantially superior cell transformation abilities (motivation) (Abstract).

In view of such benefit, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to utilize the complexing polymer as dispersing agent to produce the apatite dispersion.

Claim 4: Itoi et al. disclose an apatite dispersion (column 3 lines 53 and 54).

Claims 5 and 6: See Kumta et al. column 9, lines 5-58.

Claims 9-10: See Itoi et al. column 3, lines 53 and 54.

Claim 11: See Itoi et al. Table 1, Example 7.

Claim 12: See Itoi et al. column 3, lines 3-19.

Claim 13: See Itoi et al. column 4, line 66.

5. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Itoi et al. (US6159437) in view of Kumta et al. (US7247288).

The disclosure of Itoi et al. and Kumta et al. is adequately set forth in paragraph 4 and is incorporated herein by reference.

Itoi et al. and Kumta et al. are silent on the molar ratio of anionic functional groups in the polymer to moles of calcium in the dispersion is between 0.0001 and 0.1.

Itoi et al. further disclose the molar ratio of anionic functional groups in the sodium hexametaphosphate dispersion agent to moles of calcium in the dispersion is between 0.0001 and 0.1 (Example 7, Table 1).

Kumta et al. disclose a method for production of nanocrystalline hydroxyapatite particles comprising polymers complex calcium phosphate which include polyamino acids (column 9, lines 43-44), such as poly-L-lysine and polyacrylate (column 9, line 48). The nanocrystalline

hydroxyapatite particles exhibit substantially superior cell transformation abilities (motivation) (Abstract).

It would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to utilize the molar ratio of anionic functional groups in the polymer to manufacture the apatite dispersion.

6. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Itoi et al. (US6159437) in view of Kumta et al. (US7247288).

The disclosure of Itoi et al. and Kumta et al. is adequately set forth in paragraph 4 and is incorporated herein by reference.

Itoi et al. and Kumta et al. are silent on the molecular weight of the polymer.

The higher the molecular weight of the polymer will increase the colloidal dispersion viscosity and make it difficult to process. But if the polymer molecular is low, the hydroxyapatite will not have enough mechanical strength.

It would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to adjust the polymer molecular weight in the claimed range to obtain the composite compound having strong mechanical strength while still easy to process.

Allowable Subject Matter

7. Claims 14-19 are allowed.

8. The following is a statement of reasons for the indication of allowable subject matter: The present claims are allowed over the closet references: Itoi et al. (US6159437) and Kumta et al. (US7247288).

Itoi et al. disclose a method of producing an apatite dispersion with polymeric phosphate dispersion agents such as sodium hexametaphosphate and sodium tripolyphosphate (column 3 lines 53 and 54) and the size of the apatite particle is 10-100 nm in short-axis and 30-300 nm in long axis (a prima facie case of obviousness, since the claimed ranges "overlap or lie inside ranges disclosed by the prior art", read on claims 1-3) (column 3 lines 22-24). However, Itoi et al. fails to teach or fairly suggest the claimed method for preparing the dispersions of calcium phosphate platelets, wherein the length of the platelets, L, is between 5 and 500 nm and the thickness of the platelets is between 0.5 and 20 nm, and at least one polymer which complexes calcium comprising the steps of: i) preparing a solution of calcium salts and adjusting the pH to a selected value of between 4 and 6; ii) adding a phosphate solution to the solution obtained in step i) over a period of time of between 30 minutes and 4 hours, so as to obtain a calcium to phosphorus molar ratio of between 1 and 2.5, wherein the pH is maintained constant at the selected value of between 4 and 6 until a calcium phosphate platelet dispersion is formed; iii) heat treating the dispersion obtained in step ii) at a temperature of between 50˚C and 95˚C; iv) washing the dispersion obtained in step iii); v) adding a dispersion agent to the dispersion obtained in step iv); vi) separating the colloidal dispersion obtained in step v); wherein in at least one of steps i) or ii), the solutions further comprise ammonium ions; and wherein at least one polymer which complexes calcium is added during step i) or ii).

Kumta et al. disclose hydroxyapatite was chemically synthesized using $CaCl_2$ and Na_3PO_4 in deionized water. Stock reagent solutions were first prepared, including: 2 M calcium solution (column 18, lines 28 and 29), buffered saline (…1.5 mM Na_3PO_4…) (column 18, lines 31 and 32). The calcium solution, 20 mMoles, containing plasmid DNA was mixed with Na_3PO_4

solution, 1.5 mMoles, then incubated for either 4 or 12 hours at a pH of 7.5 and temperature of 37°C and the nanocrystalline hydroxyapatite was formed (column 18, lines 18 to 25). The solution was washed (column 18, lines 41-52). The resulting mixture can be air-dried or dried in vacuum to generate the polymeric structure containing the nanosized hydroxyapatite particles (column 22, lines 23- 29). The hydroxyapatite has Ca/P molar ration of 1.67 (column 1, line 29). Kumta et al. also disclose widely used aqueous colloidal precipitation reactions to synthesize hydroxyapatite are as follows:

$$10Ca(OH)_2+6H_3PO_4 \rightarrow Ca_{10}(PO_4)(OH)_2+18H_2O \quad \text{(Formula I)}$$

$$10Ca(NO_3)_2+6(NH_4)_2HPO_4+2H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2+12NH_4NO_3+8HNO_3 \quad \text{(Formula II)}$$

Formula II indicates the use of ammonium phosphate. However, Kumta et al. fails to teach or fairly suggest the claimed method for preparing the dispersions comprising the steps of: i) preparing a solution of calcium salts and adjusting the pH to a selected value of between 4 and 6; ii) adding a phosphate solution to the solution obtained in step i) over a period of time of between 30 minutes and 4 hours, so as to obtain a calcium to phosphorus molar ratio of between 1 and 2.5, wherein the pH is maintained constant at the selected value of between 4 and 6 until a calcium phosphate platelet dispersion is formed; iii) heat treating the dispersion obtained in step ii) at a temperature of between 50°C and 95°C; iv) washing the dispersion obtained in step iii); v) adding a dispersion agent to the dispersion obtained in step iv); vi) separating the colloidal dispersion obtained in step v); wherein in at least one of steps i) or ii), the solutions further comprise ammonium ions; and wherein at least one polymer which complexes calcium is added during step i) or ii).

There is no prior art of record, alone or in combination teach and fairly suggest the claimed method for preparing the dispersions of calcium phosphate platelets, wherein the length of the platelets, L, is between 5 and 500 nm and the thickness of the platelets is between 0.5 and 20 nm, and at least one polymer which complexes calcium. Based on the finding, the linking claims comprise the method for preparing the dispersions of calcium phosphate platelets are also allowable.

Response to Arguments

9. Applicant's arguments with respect to claims 1-19 have been considered but are moot in view of the new ground(s) of rejection.

10. Applicants' alleged: This reading of Itoi is mistaken. The particle size referred to by the examiner is the particle size of the primary particles of apatite. Itoi describes using apatite particles formed from the primary particles to produce the slurry. The particles used to form the slurry have particle sizes of 10 μm to 100 μm. Col. 3, lines 33-35.

Response: The particle sizes of 10 μm to 100 μm referred is the particle size before agitation milling. Claim 1 recites dimensions of calcium phosphate plates, i.e. primary particles, not secondary particles.

11. Applicants' alleged: 'Kumta et al. does not describe a colloidal dispersion comprising … and at least one polymer which complex calcium".

Response: Attention is drawn to column 13, lines 31-47 where Kumta et al. disclose the hydroxyapatite complex can be formulated into ointment, balm or lotion. Attention is also drawn to column 13, lines 56-67. The hydroxyapatite-DNA complex can be used alone in an aqueous solution, for instance suspended in normal saline as well as producing membrane of Example 5.

12. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun-Cheng Wang whose telephone number is (571)270-5459. The examiner can normally be reached on Monday to Friday w/alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Wu can be reached on 571-272-1114. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ling-Siu Choi/
Primary Examiner, Art Unit 1796

/Chun-Cheng Wang/
Examiner, Art Unit 1796

/CCW/